

double-patenting as unpatentable over claims 1-16 of U.S. Patent No. 5, 976,524 (the '524 patent), in view of Liu, et al. Applicant notes that the claims of the present application are directed to methods for the *in vitro* treatment of metanephric tissue with one or more growth factors prior to transplantation (claims 1, 4-5, 17, 20 and 25) and the *in vivo* treatment of metanephric tissue with one or more growth factors at the time of ureteroureterostomy (claims 7, 17, 20 and 25) or at the time of or after transplantation (claims 22, 8-9 and 23-25). Claims 1-16 of the '524 patent, in contrast, are directed to the implantation of whole metanephros into recipients. Claims 1-16 of the '524 patent do not recite the use of growth factors. However, the Examiner maintains that it would have been obvious for the skilled artisan to administer IGF-1 to metanephric tissue based on the teachings of Liu et al. so as to render the pending claims obvious.

Liu teaches the exogenous administration of IGF-1 to mouse metanephroi stored in organ culture, wherein addition of IGF-1 growth factor is correlated with metanephric enlargement and the synthesis of extracellular matrix proteoglycans. Liu, however, fails to teach (1) the contacting of metanephric tissue with one or more growth factors wherein the metanephric tissue is transplanted into a recipient (as required by claim 1, (2) the contacting of metanephric tissue with one or more growth factors in a recipient either at the time of ureteroureterostomy (as required by claim 7) or (3) the contacting of metanephric tissue in a recipient *in vivo* at the time of or after transplant (as required by claim 22). It would, therefore, not be obvious for the skilled artisan to combine the administration of IGF-1 to metanephric tissue based on the teachings of Liu et al. with the claims of the '524 patent. Applicant accordingly requests that the Examiner withdraw the outstanding rejection.

Claim Rejection – Nonstatutory Double Patenting in view of Rogers, et al.

The Examiner maintains that claims 1 (and claims 4-5, 17, 20 and 25 which depend therefrom), 7 (and claims 17, 20 and 25 which depend therefrom) and 22 (and claims 8-9 and 23-25 which depend therefrom) of the present application are rejected under the judicially created doctrine of obvious-type double-patenting as unpatentable over claims 1-16 of the '524 patent, in view of Rogers, et al. Applicant reiterates that the claims of the present application are directed to methods for the *in vitro* treatment of metanephric tissue with one or more growth factors prior to transplantation (claims 1, 4-5, 17, 20 and 25)

and the *in vivo* treatment of metanephric tissue with one or more growth factors at the time of ureteroureterostomy (claims 7, 17, 20 and 25) or at the time of or after transplantation (claims 22, 8-9 and 23-25). Claims 1-16 of the '524 patent, in contrast, are directed to the implantation of whole metanephros into recipients. Claims 1-16 of the '524 patent do not recite the administration of growth factors.

However, the Examiner maintains that it would have been obvious for the skilled artisan to exogenously administer TGF- α growth factor to metanephric tissue based on the teachings of Rogers et al.

Rogers teaches that TGF- α growth factor is endogenously produced by metanephroi grown in chemically defined organ culture. However, Roger fails to teach treatment of metanephric tissue with a solution containing one or more exogenously administered growth factors specifically demonstrated to induce metanephric tissue development. It would accordingly not be obvious for the skilled artisan to combine the exogenous administration of TGF- α growth factor with the claims of the '524 patent.

Applicant accordingly requests that the Examiner withdraw the outstanding rejection.

CONCLUSION

Applicant respectfully submits that the claims are in condition for allowance. If, upon review, the Examiner feels there are additional outstanding issues, the Examiner is invited to direct any calls in connection with this application to the undersigned at (415) 781-1989.

Respectfully submitted,

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